

# Twin preterm neonates born to a methamphetamine-using mother: divergent gastrointestinal complications — spontaneous intestinal perforation and necrotizing enterocolitis

## Abstract

Methamphetamine use during pregnancy is associated with adverse neonatal outcomes, but gastrointestinal complications are less well described. We report preterm twin neonates born at 32 weeks to a mother with polysubstance use, including methamphetamine, who developed divergent intestinal pathologies. Twin A developed spontaneous intestinal perforation requiring surgical intervention, while Twin B developed necrotizing enterocolitis managed medically. These findings suggest that prenatal stimulant exposure may predispose to intestinal ischemia, with postnatal factors influencing disease expression. This case supports the concept of an ischemia–inflammation spectrum linking SIP and NEC and highlights the importance of early recognition and individualized management in substance-exposed preterm infants.

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## Case report

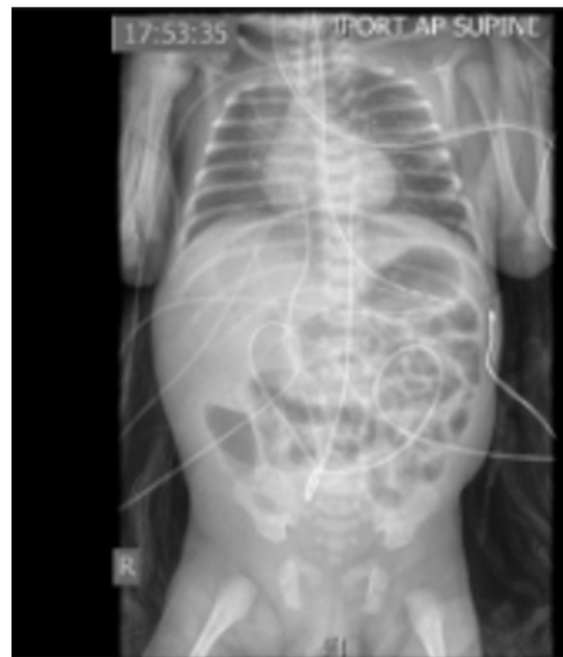
32-week gestation preterm infants were born by emergent cesarean section. The mother was a 28-year-old gravida 4, para 2 with a history of methamphetamine, cocaine, and buprenorphine use, as well as tobacco exposure and domestic abuse. Prenatal care was limited to a single visit at 27 weeks' gestation. The twins were diamniotic and dichorionic. Laboratory evaluation revealed negative screening for gonorrhea, chlamydia, syphilis, and hepatitis B, with positive hepatitis C antibody status. She was rubella nonimmune, and group B streptococcus status was unknown. She presented in preterm labor at 32 weeks' gestation and required transfer to a tertiary care center, where an emergency cesarean section was performed. Cord toxicology was positive for amphetamine and methamphetamine, confirming in-utero exposure.

Twin A, 1,680-gram male infant, was born with Apgar scores of 8 at 1 and 9 at 5 minutes. He initially required minimal respiratory support. Early sepsis evaluation was unremarkable. The feedings were started on day 1 of life and were progressively advanced as per feeding protocol. However, on day of life seven, he developed abdominal distension, mottled skin, and signs of poor perfusion. Clinical deterioration was marked by respiratory distress, metabolic acidosis, and the need for intubation and hemodynamic support. Radiographic evaluation revealed significant pneumoperitoneum with possible pneumatosis (Figure 1 & 2). On day eight, the infant developed bilious emesis, and emergent exploratory laparotomy revealed a cecal perforation (Figure 3).

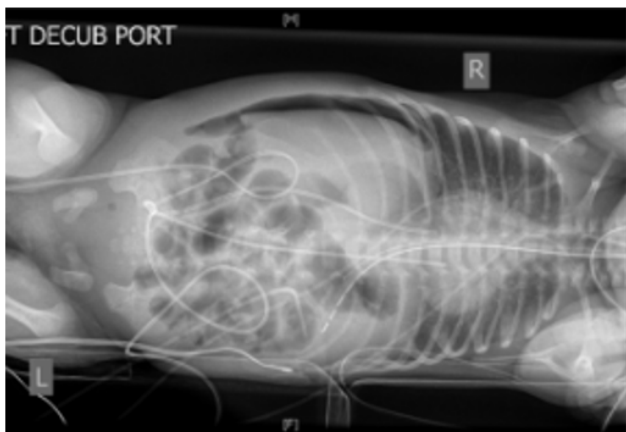
Surgical management included ileocectomy with end ileostomy. Postoperatively, he required ventilatory support and vasopressor therapy. Peritoneal cultures grew *Staphylococcus epidermidis*, and he was treated with broad-spectrum antibiotics. Gradual recovery followed, with successful advancement to full enteral feeds and no evidence of intraventricular hemorrhage or neonatal withdrawal symptoms.

In contrast, Twin B, a 1,630-gram male infant born in breech presentation, required initial respiratory support including positive-

pressure ventilation, continuous positive airway pressure, and one dose of surfactant. Enteral feeds were initiated on day one of life. On day eight, he developed mild abdominal distension and recurrent emesis. Radiographic imaging demonstrated pneumatosis intestinalis localized to the ascending colon (Figure 4), consistent with necrotizing enterocolitis (Bell's Stage II).<sup>1</sup> The infant was managed medically with bowel rest, antibiotics, and supportive care. Serial imaging showed resolution of pneumatosis without progression to perforation. Feeding was gradually reintroduced and well tolerated, and the remainder of the hospital course was uneventful, with normal cranial imaging and no signs of drug withdrawal.



**Figure 1** Twin A. Chest x-ray AP view shows a volume of intraperitoneal free air layering over the liver.



**Figure 2** Twin A. Left lateral decubitus x-ray: Free intraperitoneal air over the liver. Small focus of gas seen in the right lower quadrant suspicious for pneumatosis. Bowel gas pattern was nonobstructive.



**Figure 3** Twin A. Cecal perforation noted on exploratory laparotomy.



**Figure 4** Twin B. KUB on day 18: Pneumatosis in ascending colon

Methamphetamine use during pregnancy remains a significant and growing public health concern, associated with adverse maternal and neonatal outcomes, including prematurity, placental insufficiency, and multisystem neonatal complications.<sup>2,3</sup> Among these, gastrointestinal morbidity in preterm infants—particularly necrotizing enterocolitis (NEC) and spontaneous intestinal perforation (SIP)—is a serious and potentially life-threatening consequence.<sup>4,5</sup> Although both conditions share common risk factors, they differ in pathogenesis, timing, and clinical course. This report describes a unique case of preterm twin neonates born to a mother with polysubstance abuse, including methamphetamine, in whom one developed spontaneous intestinal perforation and the other necrotizing enterocolitis, highlighting divergent manifestations of intestinal injury within a shared intrauterine environment.

This case illustrates two distinct gastrointestinal pathologies—SIP and NEC—occurring in preterm twins exposed to methamphetamine and other substances in utero. The coexistence of these divergent conditions in genetically similar infants underscores the complex interplay between prenatal insults and postnatal factors in determining disease expression. Methamphetamine is a potent sympathomimetic agent that induces vasoconstriction through increased catecholamine activity, leading to uteroplacental insufficiency and chronic fetal hypoxia.<sup>3</sup> Placental vascular pathology, including infarction and thrombosis, has been well described in stimulant-exposed pregnancies and likely contributes to impaired fetal organ perfusion.<sup>3,6</sup>

The fetal intestine is particularly vulnerable to hypoxic-ischemic injury due to immature regulation of mesenteric blood flow. In this context, reduced perfusion can compromise mucosal integrity, disrupt barrier function, and predispose to bacterial translocation. Twin A's early presentation with focal cecal perforation is consistent with spontaneous intestinal perforation, which is thought to result from localized ischemia without significant inflammation.<sup>4</sup> In contrast, Twin B's later onset of pneumatosis following initiation of enteral feeding suggests a more complex process involving ischemia, microbial colonization, and exaggerated inflammatory responses characteristic of necrotizing enterocolitis.<sup>7,8</sup>

Rather than representing entirely separate entities, SIP and NEC may be better understood as points along an ischemia–inflammation continuum. Prenatal vascular compromise may prime the intestine for injury, while postnatal exposures such as feeding practices, microbiome development, and hemodynamic instability influence the specific clinical manifestation.<sup>7,9</sup> The absence of breast milk in Twin B may have further contributed to the development of NEC, given the protective role of human milk in modulating gut microbiota and reducing inflammation.<sup>10</sup>

Polysubstance exposure in this case likely amplified the risk of adverse outcomes. Both methamphetamine and cocaine are potent vasoconstrictors, while nicotine contributes to chronic hypoxia and impaired placental blood flow.<sup>6,11</sup> Although buprenorphine is not directly associated with vasoconstriction, it reflects a high-risk maternal environment often associated with poor nutrition and inadequate prenatal care. The combined effects of these exposures contributed to placental insufficiency and fetal vulnerability. Importantly, even in twin gestations, differences in placental sharing and blood flow may result in variable fetal exposure and outcomes.

Early radiographic evaluation and proper surgical or medical management are essential for favorable outcomes.<sup>5,12</sup> Additionally, cautious advancement of enteral feeding and close monitoring for feeding intolerance are critical in high-risk populations.

Although both infants had favorable short-term outcomes, long-term follow-up is still essential. Preterm infants with prenatal stimulant exposure are at increased risk for neurodevelopmental delay, growth impairment, and behavioral disorders.<sup>2,6</sup> Infants requiring surgical intervention, such as Twin A, also require monitoring for complications including adhesive bowel obstruction and nutritional deficiencies.

In summary, this case supports the hypothesis that prenatal methamphetamine exposure contributes to gastrointestinal morbidity through mechanisms of vascular compromise and fetal hypoxia. The divergent presentations of SIP and NEC in these twins highlight the spectrum of intestinal injury that may result from shared prenatal risk factors. Recognition of this continuum has important implications for early diagnosis, individualized management, and long-term care of substance-exposed preterm infants. This case contributes to the limited but growing body of literature linking prenatal methamphetamine exposure to neonatal gastrointestinal morbidity. It underscores the need for further research into the mechanisms of drug-induced fetal vascular injury, as well as the development of targeted preventive and management strategies. Long-term follow-up of affected infants remains critical, given the potential for neurodevelopmental impairment, growth challenges, and gastrointestinal sequelae.<sup>13–15</sup>

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## Conflicts of interest

The authors of this manuscript declare no financial or personal conflicts.

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